



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: G.A. Demopulos et al. Attorney Docket No: OMER-1-18473
Application No: 10/031,546 Group Art Unit: 1614
Filed: January 18, 2002 Examiner:
Title: SOLUTIONS AND METHODS FOR INHIBITING CARTILAGE
DEGRADATION

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Seattle, Washington 98101

April 19, 2002

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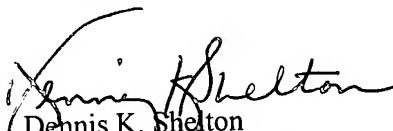
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Respectfully submitted,

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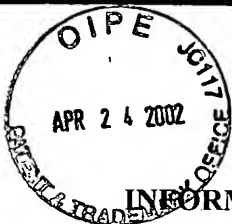
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U.S. PATENT DOCUMENTS

*Examiner Initial	ID	Document No.	Date	Name
_____	U5	5,051,443	09/24/1991	Neufeld et al.
_____	U6	5,272,139	12/21/1993	Cary, Jr.
_____	U11	4,872,865	10/10/1989	Bloebaum et al.
_____	U13	4,971,955	11/20/1990	Soll et al.
_____	U19	5,411,743	05/02/1995	Moore et al.
_____	U61	5,502,080	05/26/1996	Hitzig
_____	U62	5,618,563	04/08/1997	Berde et al.
_____	U86	5,271,961	12/21/1993	Mathiowitz et al.
_____	U136	5,605,690	02/25/1997	Jacobs et al.
_____	U164	5,800,385	09/01/1998	Demopoulos et al.
_____	U192	6,083,534	07/04/2000	Wallach et al.
_____	U218	5,270,300	12/14/1993	Hunziker
_____	U219	5,700,774	12/23/1997	Hattersley et al.
_____	U220	5,837,258	11/17/1998	Grotendorst
_____	U224	5,368,858	11/29/1994	Hunziker
_____	U225	5,393,739	02/28/1995	Bentz et al.
_____	U252	5,446,070	8/29/1995	Mantelle
_____	U256	5,480,901	1/2/1996	Baker et al.
_____	U270	5,667,764	9/16/1997	Kopia et al.
_____	U271	6,117,425	09/12/2000	MacPhee et al.
_____	U272	5,932,551	08/03/1999	Caldwell et al.

*Examiner Initial	ID	Document No.	Date	Name
	U273	5,672,583	09/30/1997	Chapman et al.
	U277	US 6,261,279 B1	07/17/2001	Demopulos et al.
	U279	US 6,197,325 B1	03/06/2001	MacPhee et al.
	U280	5,459,135	10/17/1995	Golub et al.
	U284	US 6,306,820 B1	10/23/2001	Bendele et al.
	U285	5,180,812	1/19/1993	Dower et al.
	U286	5,766,585	06/16/1998	Evans et al.
	U287	5,767,065	06/16/1998	Mosley et al.
	U290	US 6,214,049 B1	04/10/2001	Gayer et al.
	U291	5,674,844	10/07/1997	Kuberasampath et al.
	U292	6,034,062	03/07/2000	Thies et al.
	U293	5,403,952	04/04/1995	Hagmann et al.
	U332	5,972,880	10/26/1999	Pelletier et al.
	U334	5,860,950	01/19/1999	Demopulos et al.
	U341	5,591,740	01/07/1997	Chipman et al.
	U342	6,159,464	12/12/2000	Glorioso et al.

FOREIGN PATENT DOCUMENTS

*Examiner Initial	ID	Document No.	Publication Date	Country	Translation <u>Provided</u>	
					Yes	No
	F15	WO 94/06476 A1	03/31/1994	WIPO		
	F29	WO 96/26738 A1	09/06/1996	WIPO		
	F32	WO 96/11671 A1	04/25/1996	WIPO		
	F64	WO 99/65470 A1	12/23/1999	WIPO		
	F70	WO 99/62459A2	12/09/1999	WIPO		
	F86	WO 9824477 A1	06/11/1998	WIPO		
	F88	WO 00/62790 A2	10/26/2000	WIPO		
	F91	WO 00/73468 A1	12/07/2000	WIPO		
	F96	EP 0 428 573 B1	01/26/1994	European		
	F97	WO 01/47510 A2	07/05/2001	WIPO		
	F100	EP 0 500 556 B1	01/19/2001	European		X
	F101	WO 00/23072 A1	04/27/2000	WIPO		

*Examiner Initial	ID	Document No.	Publication Date	Country	Translation Provided	
					Yes	No
_____	F102	WO 00/25745 A2	05/11/2000	WIPO		
_____	F107	WO 00/56298 A2	09/28/2000	WIPO		
_____	F108	WO 96/34955 A1	11/07/1996	WIPO		

OTHER INFORMATION
(Including Author, Title, Date, Pertinent Pages, Etc.)

*Examiner Initial	ID	Document Information
_____	O129	Reuben, S.S., et al. "Postoperative Analgesia for Outpatient Arthroscopic Knee Surgery with Intraarticular Bupivacaine and Ketorolac," <i>Anesth. Analg.</i> 80 :1154-1157 (1995).
_____	O133	Sosnowski, M., et al. "Spinal Administration of Receptor-Selective Drugs as Analgesics: New Horizons," <i>J. Pain & Symptom Manag.</i> 5 :204-213 (1990).
_____	O181	Pierce, P.A., et al. "Dual Effect of the Serotonin Agonist, Sumatriptan, on Peripheral Neurogenic Inflammation," <i>Reg. Anesth.</i> 21 :219-225 (1996).
_____	O219	Allen, G.C., et al. "Postarthroscopy Analgesia with Intraarticular Bupivacaine/Morphine: A Randomized Clinical Trial," <i>Anesthesiology</i> 79 : 475-480 (1993).
_____	O225	Uysalel, A., et al. "Comparison of Intraarticular Bupivacaine with the Addition of Morphine or Fentanyl for Analgesia After Arthroscopic Surgery," <i>Arthroscopy</i> 11 : 660-663 (1995).
_____	O226	Ruwe, P.A., et al. "The Effect of Intraarticular Injection of Morphine and Bupivacaine on Postarthroscopic Pain Control," <i>Am. J. Sports Med.</i> 23 : 59-64 (1995).
_____	O228	Reuben, S.S., et al. "Postarthroscopic Meniscus Repair Analgesia with Intraarticular Ketorolac or Morphine," <i>Regional Anes. & Pain Man.</i> 82 :1036-9 (1996).
_____	O239	Tsai, L., et al. "Arthroscopic surgery of the knee in local anaesthesia: An analysis of age-related pathology," <i>Arch. Orthop. Trauma Surg.</i> 112 : 136-138 (1993).

*Examiner Initial	ID	Document Information
_____	O253	Wredmark, T., et al., "Arthroscopy Under Local Anaesthesia Using Controlled Pressure-Irrigation With Prilocaine," <i>J. Bone Joint Surg.</i> 64 :583-585 (1982).
_____	O289	Verschure, P.J., et al. "Responsiveness of articular cartilage from normal and inflamed mouse knee joints to various growth factors," <i>Ann. Rheum. Dis.</i> 53 : 455-460 (1994).
_____	O330	Band, C.J., et al. "Phosphatidylinositol 3'-Kinase and p70 ^{s6k} Are Required for Insulin but Not Bisperoxovanadium 1,10-Phenanthroline (bpV(phen)) Inhibition of Insulin-like Growth Factor Binding Protein Gene Expression: Evidence for MEK-Independent Activation of Mitogen-Activated Protein Kinase by bpV(phen)," <i>J. Biol. Chem.</i> 272 :138-145 (1997).
_____	O444	Huch, K., et al. "Effects Of Recombinant Human Osteogenic Protein 1 On The Production Of Proteoglycan, Prostaglandin E ₂ And Interleukin-1 Receptor Antagonist By Human Articular Chondrocytes Cultured In The Presence Of Interleukin-1 β ," <i>Arthritis & Rheum.</i> 40 :2157-2161 (1997).
_____	O447	Goldring, M.B., "Osteoarthritis and Cartilage: The Role of Cytokines," <i>Curr. Rheumatol. Rep.</i> 2 :459-465 (2000).
_____	O448	Jorgensen, C., et al. "Interleukin-4 And Interleukin-10 Are Chondroprotective And Decrease Mononuclear Cell Recruitment In Human Rheumatoid Synovium <i>In Vivo</i> ," <i>Immun.</i> 93 :518-523 (1998).
_____	O449	Sugiyama et al. "Interleukin 10 Cooperates With Interleukin 4 To Suppress Inflammatory Cytokine Production By Freshly Prepared Adherent Rheumatoid Synovial Cells," <i>Journ. of Rheum.</i> 22 :2020-6 (1995).
_____	O450	Van Roon, J.A.G., et al. "Prevention and Reversal of Cartilage Degradation in Rheumatoid Arthritis by Interleukin-10 and Interleukin-4," <i>Arthritis Rheum.</i> 39 :829-835 (1996).
_____	O453	Hollander, A.P., et al. "Human cartilage is degraded by rheumatoid arthritis synovial fluid but not by recombinant cytokines <i>in vitro</i> ," <i>Clin. Exp. Immunol.</i> 83 : 52-57 (1991).
_____	O490	Klareskog, L., et al. "Immunopathogenesis and immunotherapy in rheumatoid arthritis: an area in transition," <i>J. Intern. Med.</i> 238 : 191-206 (1995).

*Examiner Initial	ID	Document Information
_____	O502	McCarty, M.F., et al. "Niacinamide therapy for osteoarthritis--does it inhibit nitric oxide synthase induction by interleukin 1 in chondrocytes?," <i>Med. Hypotheses</i> 53 : 350-360 (1999) (Abstract Only).
_____	O503	Brittberg, M., et al. "Autologous chondrocyte transplantation," <i>Clin. Orthop.</i> 367 : S147-S155 (1999) (Abstract Only).
_____	O508	Pelletier, J.P., "The influence of tissue cross-talking on OA progression: role of nonsteroidal antiinflammatory drugs," <i>Osteoarthritis Cartilage</i> 7 : 374-376 (1999) (Abstract Only).
_____	O512	Chambers, M.G., et al. "Chondrocyte cytokine and growth factor expression in murine osteoarthritis," <i>Osteoarthritis Cartilage</i> 5 : 301-308 (1997) (Abstract Only).
_____	O516	Verschure, P.J., et al. "Articular cartilage destruction in experimental inflammatory arthritis: insulin-like growth factor-1 regulation of proteoglycan metabolism in chondrocytes," <i>Histochem. J.</i> 28 : 835-857 (1996).
_____	O518	Aigner, T., et al. "Inflammatory cytokine mediated anti-anabolic effects: a potential mechanism in rheumatoid cartilage degeneration," <i>Verh. Dtsch. Ges. Pathol.</i> 80 : 282-287 (1996) (Abstract Only).
_____	O520	Trippel, S.B., "Growth factor actions on articular cartilage," <i>J. Rheumatol. Suppl.</i> 43 : 129-132 (1995) (Abstract Only).
_____	O521	Lotz, M., et al. "Cytokine regulation of chondrocyte functions," <i>J. Rheumatol. Suppl.</i> 43 : 104-108 (1995) (Abstract Only).
_____	O523	Homandberg, G.A., et al. "High concentrations of fibronectin fragments cause short-term catabolic effects in cartilage tissue while lower concentrations cause continuous anabolic effects," <i>Arch. Biochem. Biophys.</i> 311 : 213-218 (1994) (Abstract Only).
_____	O524	Sah, R.L., et al. "Differential effects of bFGF and IGF-I on matrix metabolism in calf and adult bovine cartilage explants," <i>Arch. Biochem. Biophys.</i> 308 : 137-147 (1994) (Abstract Only).
_____	O533	Mohamed-Ali, H. "Proteolytic enzymes and the destruction of articular cartilage in arthritis and chronic polyarthritis," <i>Wien. Med. Wochenschr.</i> 141 : 77-85 (1991) (Abstract Only).

*Examiner Initial	ID	Document Information
_____	O534	Venn, G., et al., "Effects of catabolic and anabolic cytokines on proteoglycan biosynthesis in young, old and osteoarthritic canine cartilage," <i>Biochemical Society Transactions</i> , Vol. 18, pp. 973-974, 1990.
_____	O535	Lanzer, W.L., et al. "Changes in articular cartilage after meniscectomy," <i>Clin. Orthop.</i> 252 : 41-48 (1990) (Abstract Only).
_____	O540	Herman, J.H., et al. "Immunologic modulation of cartilage metabolism," <i>J. Rheumatol.</i> 14 : 83-85 (1987) (Abstract Only).
_____	O542	Hess, E.V., et al. "Cartilage metabolism and anti-inflammatory drugs in osteoarthritis," <i>Am. J. Med.</i> 81 : 36-43 (1986) (Abstract Only).
_____	O548	Vidal y Plana, R.R., et al. "Glucosamine: its importance for the metabolism of articular cartilage. 2. Studies on articular cartilage," <i>Fortschr. Med.</i> 98 : 801-806 (1980) (Abstract Only).
_____	O638	Shalom-Barak, T., et al. "Interleukin-17-induced Gene Expression in Articular Chondrocytes is Associated with Activation of Mitogen-activated Protein Kinases and NF- κ B," <i>J. Biol. Chem.</i> 273 : 27467-27473 (1998).
_____	O645	Tardif, G., et al. "Collagenase 3 production by human osteoarthritic chondrocytes in response to growth factors and cytokines is a function of the physiologic state of the cells," <i>Arthritis Rheum.</i> 42 : 1147-1158 (1999) (Abstract only).
_____	O710	Dingle, J.T. "Cartilage Maintenance in Osteoarthritis: Interaction of Cytokines, NSAID and Prostaglandins In Articular Cartilage Damage and Repair," <i>J. Rheumatol. Suppl.</i> 28 : 30-37 (1991).
_____	O719	Attur, M.G., et al. "Tetracycline Up-Regulates COX-2 Expression and Prostaglandin E ₂ Production Independent of its Effect on Nitric Oxide," <i>J. Immunol.</i> 162 : 3160-3167 (1999).
_____	O734	Blanco, F.J., et al. "Chondrocyte apoptosis induced by nitric oxide," <i>Am. J. Pathol.</i> 146 : 75-85 (1995) (Abstract only).
_____	O742	Attur, M.G., et al. "Autocrine Production of IL-1 β by Human Osteoarthritis-Affected Cartilage and Differential Regulation of Endogenous Nitric Oxide, IL-6, Prostaglandin E ₂ , and IL-8," <i>Proc. Assoc. Am. Physicians</i> 110 : 65-72 (1998).

*Examiner Initial	ID	Document Information
_____	O745	Lubberts, E. et al. "Reduction of Interleukin-17-Induced Inhibition of Chondrocyte Proteoglycan Synthesis in Intact Murine Articular Cartilage by Interleukin-4," <i>Arthritis Rheum.</i> 43 : 1300-1306 (2000).
_____	O747	Martel-Pelletier, J., et al. "Mitogen-activated protein kinase and nuclear factor κ B together regulate interleukin-17-induced nitric oxide production in human osteoarthritic chondrocytes: possible role of transactivating factor mitogen-activated protein kinase-activated protein [sic] kinase (MAPKAPK)," <i>Arthritis Rheum.</i> 42 : 2399-2409 (1999) (Abstract only).
_____	O752	Agro, A., et al. "Prostaglandin E2 enhances interleukin 8 (IL-8) and IL-6 but inhibits GM-CSF production by IL-1 stimulated human synovial fibroblasts in vitro," <i>J. Rheumatol.</i> 23 : 862-868 (1996) (Abstract only).
_____	O758	Kawamura, M., et al. "Growth factors, mitogens, cytokines, and bone morphogenetic protein in induced chondrogenesis in tissue culture," <i>Dev. Biol.</i> 130 : 435-442 (1988) (Abstract only).
_____	O773	Chandrasekhar, S., et al. "Degradative and repair responses of cartilage to cytokines and growth factors occur via distinct pathways," <i>Agents Actions Suppl.</i> 39 : 121-125 (1993) (Abstract only).
_____	O774	Harvey, A., et al. "Differential modulation of degradative and repair responses of interleukin-1-treated chondrocytes by platelet-derived growth factor," <i>Biochem. J.</i> 292 : 129-136 (1993) (Abstract only).
_____	O780	Stevens, P., et al. "Synergism of basic fibroblast growth factor and interleukin-1 beta to induce articular cartilage-degradation in the rabbit," <i>Agents Actions</i> 34 : 217-219 (1991) (Abstract only).
_____	O781	Chandrasekhar, S., et al. "Differential regulation of metalloprotease steady-state mRNA levels by IL-1 and FGF in rabbit articular chondrocytes," <i>FEBS Lett.</i> 296 : 195-200 (1992) (Abstract only).
_____	O786	Van Der Kraan, P., et al. "Role of nitric oxide in the inhibition of BMP-2-mediated stimulation of proteoglycan synthesis in articular cartilage," <i>Osteoarthritis Cartilage</i> 8 : 82-86 (2000).
_____	O815	Glasser, R.S., et al., "The Perioperative Use Of Corticosteroids And Bupivacaine In The Management Of Lumbar Disc Disease," <i>J. Neurosurg.</i> 78 : 383-387 (1993).

*Examiner Initial	ID	Document Information
_____	O844	Van den Berg, W.B., et al. "Tissue Engineering, Cells, Scaffolds, and Growth Factors: Growth factors and cartilage repair," <i>Clin. Orthop.</i> 391S :S244-50 (2001).
_____	O846	Rogachefsky, R.A., et al. "Treatment Of Canine Osteoarthritis With Insulin-Like Growth Factor-1 (IGF-1) And Sodium Pentosan Polysulfate," <i>Osteoarthritis & Cartilage</i> 1 :105-14 (1993).
_____	O847	Goldring, M.B., et al., "Etodolac Preserves Cartilage-Specific Phenotype in Human Chondrocytes: Effects On Type II Collagen Synthesis and Associated mRNA Levels," <i>Euro. J. Rheum. & Inflamm.</i> 10 :10-21 (1990).
_____	O848	Itayem, R., et al. "Ultrastructural Studies On The Effect Of Transforming Growth Factor- β 1 On Rat Articular Cartilage," <i>APMIS</i> 105 :221-8 (1997).
_____	O849	Bhargava, M.M. et al. "The Effect Of Cytokines On The Proliferation And Migration Of Bovine Meniscal Cells," <i>Am. Jour. Sports Med.</i> 27 :636-43 (1999).
_____	O855	Goldring, M.B. "Anticytokine therapy for osteoarthritis," <i>Expert. Opin. Biol. Ther.</i> 1 :817-829 (2001).
_____	O863	Nasatzky, E., et al. "Parathyroid Hormone And Transforming Growth Factor- β 1 Coregulate Chondrocyte Differentiation <i>In Vitro</i> ," <i>Endocrine</i> 13 :305-13 (2000) (Abstract Only).
_____	O864	Heiner, John P. "Bone Formation Within Acetabular Defects In Total Hip Arthroplasty," <i>Citations from Federal Research in Progress (FRP)</i> FRP 02-01 128953, NDN-049-0233-4208-2 (Date Unknown).
_____	O866	Frisbie, D.D., et al. "Metabolic And Mitogenic Activities Of Insulin-Like Growth Factor-1 In Interleukin-1-Conditioned Equine Cartilage," <i>Am. J. Vet. Res.</i> 61 :436-441 (2000).
_____	O869	Frisbie, D.D., et al. "Treatment Of Experimental Equine Osteoarthritis By <i>In Vivo</i> Delivery Of The Equine Interleukin-1 Receptor Antagonist Gene," <i>Gene Ther.</i> 9 :12-20 (2002).
_____	O876	Gatt, C.J., et al. "Preemptive Analgesia: Its Role and Efficacy in Anterior Cruciate Ligament Reconstruction," <i>Am. J. Sports Med.</i> 26 : 524-529 (1998).

*Examiner

Initial

ID

Document Information

O877

Dingle, J.T. "The Effects of NSAID on the Matrix of Human Articular Cartilages," *Z. Rheumatol.* **58**:125-129 (1999).

Examiner

Date Considered

*Examiner: Initial if reference considered, whether or not citation is in conformance with M.P.E.P. § 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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